L10 ANSWER 11 OF 31 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:557643 CAPLUS
DOCUMENT NUMBER: 127:233558
TITLE: Use of leukotriene B4 or its analogs as antiviral and antineoplastic agents
INVENTOR(S): Gosselin, Jean; Borgeat, Pierre
PATENT ASSIGNEE(S): Virocell Inc., Can.
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9729751	A1	19970821	WO 1997-CA99	19970212
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5789441	A	19980804	US 1997-798937	19970211
AU 9715867	A1	19970902	AU 1997-15867	19970212
EP 881900	A1	19981209	EP 1997-902124	19970212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9707535	A	20000104	BR 1997-7535	19970212
JP 2000505435	T2	20000509	JP 1997-528847	19970212
PRIORITY APPLN. INFO.:			US 1996-602059	19960215
			US 1997-798937	19970211
			WO 1997-CA99	19970212

AB The present invention relates to the use of **leukotriene B4** (LTB4), variants and derivs. thereof as a therapeutic agent in the **treatment** or prophylaxis of viral **infections** caused by human and animal viruses. The present invention also relates to the use of LTB4, variants and derivs. thereof as an anti-neoplastic agent in the prophylaxis and **treatment** of cancers induced by tumor viruses and in other neoplastic diseases. The human and animal viruses are DNA viruses (e.g. parvoviridae, papovaviridae, adenoviridae, herpesviridae, poxviridae and hepadnaviridae), RNA viruses (e.g. picornaviridae, togaviridae, orthomyxoviridae, paramyxoviridae, coronaviridae, reoviridae, oncornaviridae and filoviridae in general), and Retroviridae (e.g. HIV-1 and HIV-2).

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L10 ANSWER 31 OF 31 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 88218233 MEDLINE
DOCUMENT NUMBER: 88218233
TITLE: The treatment of tinea with topically applied leukotriene B4.
AUTHOR: Katayama H
CORPORATE SOURCE: Department of Dermatology, Jichi Medical School, Tochigi-ken, Japan..
SOURCE: PROSTAGLANDINS, (1987 Dec) 34 (6) 797-804.
Journal code: Q76. ISSN: 0090-6980.
PUB. COUNTRY: United States
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198808

AB Important roles of neutrophils as well as lymphocytes against invasive fungi has been suggested. **Leukotriene B4** (LTB4) is a potent chemoattractant for neutrophils and its topical application to human skin has already been performed without serious side effects, forming intraepidermal neutrophil abscesses. Thus topical LTB4 therapy for tinea was attempted in a randomized, placebo-controlled study. LTB4 (100-900 ng depending on the area of each lesion) was applied to a whole lesion once a week until, as a rule, complete clearing was observed but maximum for 2 weeks (vesiculobullous type lesions), 5 weeks (patches with or without raised borders) or 7 weeks (macerated lesions between toes). As a result, 16 of 18 lesions **treated** with LTB4 were cleared either completely (13) or partially (3). In contrast, only 2 of 18 lesions **treated** with vehicle (50% ethanol) were cleared partially. Statistical analysis with chi 2 test revealed a significant efficacy of LTB4 over vehicle. Topical LTB4 will be used as a powerful antifungal regimen. LTB4 has not been used for **infectious** diseases before.

L10 ANSWER 24 OF 31 MEDLINE
ACCESSION NUMBER: 93331158 MEDLINE
DOCUMENT NUMBER: 93331158
TITLE: Intraperitoneal administration of leukotriene B4 (LTB4) and
omega-guanidino caproic acid methane sulfonate (GCA) increased the survival of mice challenged with methicillin-resistant Staphylococcus aureus (MRSA).
AUTHOR: Yamamoto S; Adjei A A; Kise M
CORPORATE SOURCE: Department of Nutrition, University of the Ryukyus Okinawa,
Japan..
SOURCE: PROSTAGLANDINS, (1993 Jun) 45 (6) 527-34.
Journal code: Q76. ISSN: 0090-6980.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199310

Adonis

AB **Infections** caused by methicillin-resistant Staphylococcus aureus (MRSA) very often complicate management of immunocompromised patients. We studied the effect of **leukotriene B4** (LTB4) and epsilon-guanidino caproic acid methane sulfonate (GCA), on MRSA **infection**. Mice fed a 20% casein diet were intraperitoneally administered LTB4, GCA, or saline (control) daily for 30 days. On the 10th day of this **treatment**, mice were challenged with MRSA. The survival rate in the control group (20%) was significantly lower than the rates in the GCA (60%) and LTB4 (50%) groups, respectively ($p < 0.05$). There was a significant reduction of MRSA in the spleen and kidney of the survived mice in GCA group as against mice in the LTB4 and saline groups, indicating a better recovery in GCA group than the other groups. The results suggest that intraperitoneal administration of GCA and LTB4 may play a role in host defense mechanism during MRSA **infections**.

L10 ANSWER 27 OF 31 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 91289318 MEDLINE
DOCUMENT NUMBER: 91289318
TITLE: [Effect of ketotifen on the eicosanoid system, immunoreactivity and bronchial patency in patients with obstructive pulmonary diseases].
Vliianie ketotifena na sistemu eikozanoidov, immunologicheskuiu reaktivnost' i bronkhial'nuiu prokhodimost' u bol'nykh s obstruktivnymi zabolevaniiami legkikh.
AUTHOR: Efimov V V; Blazhko V I; Liashenko M M; Voeikova L S; Bondar' T N
SOURCE: TERAPEVTICHESKII ARKHIV, (1991) 63 (3) 70-3.
Journal code: VLU. ISSN: 0040-3660.
PUB. COUNTRY: USSR
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199110

AB A study was made of the effect of ketotifen on the concentration of **leukotriene B4**, prostacyclin and thromboxane A2 in the liquid of bronchoalveolar lavage and on external respiration and cellular immunity during 4 weeks of the **treatment** of patients with **infection**-dependent bronchial asthma and chronic obstructive bronchitis. Inclusion of ketotifen into the **treatment** of patients with bronchial obstruction exerts a stimulating action on the suppressor component of T-cell immunity, leads to a decrease of the content of **leukotriene B4** and thromboxane A2 in the lavage liquid, which is accompanied by positive shifts in the clinical course of the broncho-obstructive syndrome. Ketotifen turned out most effective in patients with an initially low content of the subpopulation of T suppressors and with high concentrations of **leukotriene B4** and thromboxane A2 in the liquid of bronchoalveolar lavage.

L10 ANSWER 10 OF 31 MEDLINE
ACCESSION NUMBER: 1999027751 MEDLINE
DOCUMENT NUMBER: 99027751
TITLE: Inhibition of cytokine production and arachidonic acid metabolism by eucalyptol (1.8-cineole) in human blood monocytes in vitro.
AUTHOR: Juergens U R; Stober M; Vetter H
CORPORATE SOURCE: Abteilung Pneumologie, Medizinische Universitats-Poliklinik
Bonn, Wilhelmstrasse 35-37, D-53111 Bonn, Germany.
SOURCE: EUROPEAN JOURNAL OF MEDICAL RESEARCH, (1998 Nov 17) 3 (11) 508-10.
Journal code: COQ. ISSN: 0949-2321.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY WEEK: 19990401

AB Cineole (eucalyptol) is the isolated active agent of eucalyptus oil. Traditionally, it is recommended for **treating** the symptoms of airway diseases exacerbated by **infection**. We have examined the inhibitory effect of 1.8-cineole on LPS-and IL1beta-stimulated mediator production by human monocytes in vitro. For the first time, we report on a dose-dependent and highly significant inhibition of production of tumor necrosis factor-alpha, interleukin-1beta, **leukotriene B4** and thromboxane B2 by 1.8-cineole. In summary, this is the first report on a new mechanism of action of monoterpenes suggesting 1.8-cineole as a strong inhibitor of cytokines that might be suitable for longterm **treatment** of airway inflammation in bronchial asthma and other steroid-sensitive disorders.

ILL Req 7/24

L10 ANSWER 20 OF 31 MEDLINE
ACCESSION NUMBER: 95022857 MEDLINE
DOCUMENT NUMBER: 95022857
TITLE: Impaired leukotriene B4 release by neonatal polymorphonuclear leukocytes.
AUTHOR: Viggiano D; Romano G; Caniglia M; Santoro P; Palumbo A; Ciccimarra F
CORPORATE SOURCE: Department of Pediatrics, University Federico II, Naples, Italy..
SOURCE: PEDIATRIC RESEARCH, (1994 Jul) 36 (1 Pt 1) 60-3. Journal code: OWL. ISSN: 0031-3998.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199501

AB **Leukotriene B4** (LTB4) is a potent mediator of inflammation generated by polymorphonuclear leukocytes (PMN) in response to an appropriate stimulus. It acts as a chemoattractant and stimulates PMN functions, amplifying their inflammatory response. Newborn infants show an increased susceptibility to **infections** in which PMN dysfunctions play the main role. In this work, LTB4 release from neonatal polymorphonuclear cells was assessed to investigate whether a defect was detectable. Blood was obtained from the umbilical cord of 10 full-term healthy neonates and 10 adult controls. The LTB4 production from purified PMN suspensions was induced by three different stimuli: the calcium ionophore A23187, serum-**treated** zymosan, and formyl-methionyl-leucyl-phenylalanine at final concentrations of 2 microM, 10 mg/mL, and 10 microM, respectively. The kinetics of LTB4 release were studied for up to 30 min by assaying the supernatants of the stimulated cells with a specific RIA. The LTB4 release, undetectable in resting PMN, was strongly stimulated by the A23187, peaking at 5 min, with significantly higher levels (t test, $p < 0.01$) in newborn than in adult PMN preparations (mean +/- SD: 12.46 +/- 2.96 and 6.21 +/- 2.09 ng/10(6) cells, respectively). In comparison, serum-**treated** zymosan-stimulated PMN released smaller amounts of LTB4. The levels peaked at 10 min and were significantly (t test, $p < 0.01$) lower in newborn than in adult samples (mean +/- SD: 0.71 +/- 0.22 and 3.19 +/- 1.06 ng/10(6) PMN, respectively). Finally, when the PMN were stimulated by formyl-methionyl-leucyl-phenylalanine, the release of LTB4 was highly variable both in newborn and in adult samples, as previously reported. (ABSTRACT TRUNCATED AT 250 WORDS)

L10 ANSWER 17 OF 31 MEDLINE
ACCESSION NUMBER: 95069319 MEDLINE
DOCUMENT NUMBER: 95069319
TITLE: Association between neutrophil functions and periparturient disorders in cows.
AUTHOR: Cai T Q; Weston P G; Lund L A; Brodie B; McKenna D J; Wagner W C
CORPORATE SOURCE: Department of Veterinary Biosciences, College of Veterinary Medicine, University of Illinois, Urbana 61801..
SOURCE: AMERICAN JOURNAL OF VETERINARY RESEARCH, (1994 Jul) 55 (7) 934-43.
Journal code: 40C. ISSN: 0002-9645.
PUB. COUNTRY: United States
(CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199502

AB Neutrophil functions were examined in healthy periparturient dairy cows (n = 46) and in cows with retained placenta and metritis complex (n = 20); metritis (n = 18); or mastitis (n = 13). Blood samples (50 ml) were collected from each cow via jugular vein twice weekly from 1.5 weeks before to 4 weeks after parturition. Neutrophil function was evaluated, using 6 tests: random migration, chemotaxis, ingestion, myeloperoxidase activity (iodination), superoxide production (cytochrome C reduction), and antibody-dependent cell-mediated cytotoxicity. Ability to ingest bacteria and random migration activity of neutrophils from clinically normal cows were high around parturition and increased immediately after parturition, whereas myeloperoxidase activity and antibody-dependent cell-mediated cytotoxicity ability of neutrophils from these cows decreased after parturition. Measurement of neutrophil function in 4 ovariectomized cows revealed significant ($P < 0.0005$) seasonal changes in results of all 6 functional assays. We observed various defects of neutrophil function in all cows with abnormal conditions after parturition. Before parturition, superoxide production activity by neutrophils from cows with metritis and chemotaxis by neutrophils from cows with mastitis were significantly ($P < 0.001$ and $P < 0.05$, respectively) lower, indicating that a defect of neutrophil function may be a predisposing factor in the development of these disorders. In conclusion, the host defense role of neutrophils in periparturient cows was impaired, principally because of a defect in killing capacity, which may increase susceptibility to **infections**. We also investigated the in vitro effects of arachidonic acid metabolites and recombinant human colony-stimulating factors (rhCSF) on functions of neutrophils from clinically normal and postparturient cows with abnormalities, including retained placenta, metritis, or mastitis (n = 5/group). Each abnormal cow was matched for postpartum period with a clinically normal cow. Neutrophils from individual cows were preincubated with arachidonic acid metabolites (prostaglandin F2 alpha, 10(-7) M; prostaglandin E2, 10(-6) M; **leukotriene B4**, 10(-8) M; and lipoxin B, 10(-8) M) and rhCSF (rh-granulocyte-CSF, 1,000 or 6,000

U/ml; rh-granulocyte-macrophage-CSF, 5 or 15 ng/ml) in a 37 C water bath for 30 minutes before submitting them to function assays. There was no response by neutrophils from either clinically normal or abnormal postparturient cows to **treatment** with either arachidonic acid metabolites or rhCSF in any of the 6 functional assays. However, preincubation of neutrophils alone in a 37 C water bath for 30 minutes resulted in some alteration of neutrophil function.(ABSTRACT TRUNCATED AT 400 WORDS)